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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,996	06/11/2007	Yechiel Shai	SHAI8	3380

1444 7590 04/10/2009

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
04/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,996	SHAI, YECHIEL	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 43-51* is/are pending in the application.

4a) Of the above claim(s) *4-17 and 43-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/08, 6/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 (claims 1-22) and the peptide species as SEQ ID NO:23 in the reply filed on 2/17/09 is acknowledged. The traversal is on the ground(s) that the unity is not destroyed because the present claims are directed only to diastereomeric peptides. Applicants argue that the present invention discloses that the recognition between a transmembrane domain and a peptide within the cell membrane is not essential.

Applicants arguments have been considered but are not found persuasive

Although applicants argue that the present claims are directed only to diastereomeric peptides, the instant claims expressly recite 'diastereomeric active fragments, derivatives, analogs, or salts thereof'. As such, the claims are drawn to analogs and derivatives which are taught by the prior art. Although the specification (page 12) provides a definition for 'diastereomeric peptide' such definition is separate and distinct from derivatives, analogs, and diastereomeric active fragments. Further, it is noted that applicant points to sections 0011-0013 of the PGPub. However, limitations from the specification are not read into the claims.

Although Applicants argue that the present invention discloses that the recognition between a transmembrane domain and a peptide within the cell membrane is not essential, it is noted that the instant claims are drawn to peptides not the recognition of particular mechanisms of interaction.

The requirement is still deemed proper and is therefore made FINAL.

As discussed below, the applicants elected species as currently interpreted is obviated by the prior art. Any art that reads on non-elected species that was uncovered in the search for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species and claims to the nonelected species held withdrawn from consideration.

As noted by the applicant claims 1-3,18-22 read on the elected species. Claims 4-17 read on different peptides and claims 43-51 are drawn to a different group.

Claims 4-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/17/09.

Claims 43-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/17/09.

Claims 23-42 have been cancelled.

Claims 1-3,18-22 are under consideration.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 9/8/08 and 6/27/07 have been considered. It is noted that both IDS statements recite patent 6133413 which is listed as having Bolognesi at the author. However, 6133413 is by Mouri et al.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/530,899 (12/22/03), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, claims 18-21 are drawn to peptides wherein the bacterial protein is aspartate Tar receptor and peptides of specific sequences (SEQ ID NO:20,22-23).

Lack of Ipsis Verbis Support

Application No. 60/530,899 is void of support for peptides wherein the bacterial protein is aspartate Tar receptor or peptides of specific sequences (SEQ ID NO:20,22-23).

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/530,899 recites a genus of peptides (claim 1). However, the specification does not recite SEQ ID NO:20,22-23 nor does the specification refer to embodiments in which the bacterial protein is aspartate Tar receptor.

From the disclosure of Application No. 60/530,899 there is nothing to lead one to SEQ ID NO:20,22-23 or embodiments in which the bacterial protein is aspartate Tar receptor. As such, one would not conclude that Application No. 60/530,899 provides adequate support for the instant claims.

It is noted that section 706.02 VI D of the MPEP sets forth the method to determine the effective filing date. In particular, 'If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.'. In the instant case, claims 1-3,22 are fully supported by the provisional Application No. 60/530,899. However, claims 18-21 are not fully supported by the provisional application. As such, for purposes of searching for prior art, a priority date of 12/22/04 is used for claims 18-21.

Claim Objections

Claim 21 is objected to because of the following informalities:

Claim 21 states 'according to claims 19'. There appears to be a grammatical error. The word 'claims' should be replaced with the word 'claim'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 refers to 'diastereomeric peptide' and 'diastereomeric active fragments, derivatives, analogs or salts thereof'. It is noted that 'diastereomeric peptide' is clearly defined on page 12 of the specification. However, there is no specific definition provided for 'diastereomeric active fragments'. Diastereomeric is typically a term used to describe pairs of peptides, not a single peptide. A definition of diastereomers as recited in McMurry (Organic Chemistry see attachment) is that diastereomers have opposite configurations at some (one or more) stereogenic centers, but have the same configuration at others. In terms of the instant claims, the specific characteristics or identifying characteristics of a 'diastereomeric active fragments' are unclear. Since diastereomers occur in pairs and the claim is drawn to a peptide

(not peptides or a composition) the term diasteroemeric as currently used with respect to active fragments is unclear. There is more than one reasonable interpretation of what falls within the scope of the claims. Although the specification (page 12) provides a definition for 'diastereomeric peptide' such definition is separate and distinct from derivatives, analogs, and diastereomeric active fragments

Further, the term "active" in claim 1 is a relative term which renders the claim indefinite. The term "active" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

It is noted that claim 1 also recites derivatives and analogs. The specification states that the derivatives and analogs can have deletions, substitutions, and/or extension (page 14 lines 29-31) and that the substitutions can be non-conservative. The specification states that a derivative can have one or more residues derivatized (page 16 lines 7-10). However, the scope of analogs and derivatives is unclear. Although the specification recites a limited number of examples, exemplification is not a precise definition. There is not a standard art-recognized definition of analogs and derivatives. As such, it is unclear what structural features, if any, are required by the analogs and derivatives. There is more than one reasonable interpretation of what falls within the scope of the claims.

Claim 19 states that the peptide comprises SEQ ID NO:20. It is noted that the sequence listing provided by applicant (see also page 8 of the specification) does not denote the presence of any D-amino acids in SEQ ID NO:20 (i.e. MVLGVFALLQLISGSL). Claim 21 depends on claim 19 and states that the peptide can comprise SEQ ID NO:23 for example. SEQ ID NO:23 is

KKKMVLGVFALLdQLISGdSLKK where d denotes D-amino acid. The scope of the claims is unclear because claim 19 comprises a peptide where Q is an L-amino acid and S is an L-amino acid. However, claim 21 states that Q is a D-amino acid and S is a D-amino acid. It is noted that claim 1 states that the diastereomeric peptides comprise at least 2 D-isomers. As such, there seems to be an inconsistency in the claims since Q and S can not simultaneously be L-amino acids and D-amino acids. As such, the scope of claim 19 and dependent claims 20-21 is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3,18,22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by

> describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of replacements. It is not within the skill of the art to predict any and all replacements and any and all fragments that would inhibit functional assembly of transmembrane proteins.

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to diastereomeric peptides (defined on page 12) and fragments, derivatives and analogs thereof. Although unclear (see 112 2nd), for purposes of examination the phrase 'diastereomeric active fragments, derivatives, analogs or salts thereof' has been given the broadest reasonable interpretation. In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids. Although unclear (see 112 2nd), for purposes of examination claim 19 has been interpreted such that SEQ ID NO:20 can include D-amino acids. Claim 1 recites that the peptide can comprise 7 to 50 amino acids. In considering the size of the genus, if, for example 15 amino acids were replaced with any of the 20 naturally occurring amino acids (i.e. analogs and derivatives) there are at least 20^{15} (i.e. 32768000000000000000) different compounds. Further, there are many non-natural amino acids and other chemical compounds that could be considered analogs or derivatives. Further, there are many possible fragments. As such, the genus is large. It is noted that dependent claims 2-3 refer to diastereomeric peptides and claim 3 specifically recites classes of proteins. The genus of claims 2-3 includes any peptide comprising 7-50 amino acids of the wide range of transmembrane proteins. Claim 18 refers to a specific transmembrane protein. The genus of claim 18 includes peptides such as residues 1-7,2-8,3-9, 1-10,.....501-507 of the aspartate Tar receptor. There is no specific common core for the peptides of claim 18. As such, the genus of peptides is large. The specification includes a total of 29 sequences. Such 29 sequences are not representative of the diversity of claim 1. With respect to claim 18, the specification (page 8) recites a few sequences that appear to be from residues 13-28 of an aspartate Tar receptor. However, such peptides are not representative of any and all

peptide fragments of the aspartate Tar receptor. For example, the peptide comprising residues 13-28 does not necessarily share any structural features with peptides that comprise residues 113-138 or 213-238 or 313-338 or 413-438 for example. Taken together, the peptides represent a small fraction of the possible variety of peptides in the genus. One of skill in the art would not recognize that applicant was in possession of the claimed genus.

There is substantial variability in the genus. Since there are a substantial variety of componds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 recites that the peptide is capable of binding the transmembrane protein thereby inhibiting functional assembly. Claim 1 also refers to active fragments. However, there is no specific disclosed correlation between structure and function. It is unclear what structural elements are required for the recited function. There are no common attributes or characteristics that identify peptides capable of binding the transmembrane protein thereby inhibiting functional assembly or common attributes of active fragments. As such, one of skill in the art would not recognize a core structure, common attributes, or features of the peptides. One of skill in the art would not recognize peptides capable of binding the transmembrane protein thereby inhibiting functional assembly or active fragments outside of those specifically identified. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind the transmembrane protein thereby inhibiting functional assembly. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there

is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention/actual reduction to practice:

The specification (page 32 for example) describes the making of peptides. However, such peptides are not representative of the instant genus nor do the compounds provide a specific correlation between structure and function such that one could identify any and all peptides capable of binding the transmembrane protein thereby inhibiting functional assembly or identify active fragments.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-3,18,22 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the

specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Although unclear (see 112 2nd), for purposes of examination the phrase 'diastereomeric active fragments, derivatives, analogs or salts thereof' has been given the broadest reasonable interpretation. In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids.

Although unclear (see 112 2nd), for purposes of examination claim 19 has been interpreted such that SEQ ID NO:20 can include D-amino acids.

The specification teach that the peptides are from naturally occurring proteins (page 4-5 connecting paragraph). The claims state that the peptide comprises about 7 to 50 amino acids. As such, the peptides are open to peptides longer than 50 amino acids (see MPEP section 2111.03).

In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids. As such, the

analogs/derivatives read on the naturally occurring E. coli aspartate receptor (see abstract of Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08) for example). Further, it is noted that there are known naturally occurring peptides that have D-amino acids.

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08).

Melnyk teach biophysical studies of transmembrane domains of integral membrane proteins (abstract). Melnyk recognizes that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and other transmembrane domains and also transmembrane segments from glycophorin A (abstract). Melnyk teach the Tar-1 helix as the oligomeric determinant for the Tar protein and that the approach can be used to elucidate details of transmembrane domain folding (abstract).

Melnyk teach that the E. coli aspartate receptor transmembrane domain peptides were designed based on predictions of which residues occur in the protein transmembrane segment (see Table 2 caption). Melnyk teach that the peptides were synthesized with N and C-terminal lysines (page 11109 2nd column and Table 2). Melnyk teach the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK (Tar (TM-1) 6K-Tar-1). Melnyk teach that the peptide was used in a composition (Figures 3-4 for example).

Although unclear (see 112 2nd), for purposes of examination the phrase 'diastereomeric active fragments, derivatives, analogs or salts thereof' has been given the broadest reasonable interpretation. In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids.

Although unclear (see 112 2nd), for purposes of examination claim 19 has been interpreted such that SEQ ID NO:20 can include D-amino acids.

In the instant case, the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK of Melnk is considered a derivative/analog as recited in claim 1 wherein L-amino acids are

substituted for D-amino acids. In other words, the analogs/derivatives of claim 1 are interpreted as not requiring any D-amino acids. Since the peptide of Melnyk is taught to be from the transmembrane domain of the E. coli aspartate receptor such peptide meets the limitations of claim 1 as currently interpreted. It is noted that the peptide of Melnyk comprises the residues of SEQ ID NO:20 of the instant invention. However, since claim 19 is drawn to diastereomeric peptides (see definition page 12 of specification) and not analogs/derivatives the peptide of Melnyk does not expressly read on claim 19.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3,18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08) and Bolognesi et al (US 5,464,933 as cited in IDS 9/8/08) and Gerber et al (JMB v322 2002 pages 491-495 as cited in IDS 9/8/08).

As discussed above, Melnyk teach biophysical studies of transmembrane domains of integral membrane proteins (abstract). Melnyk recognizes that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments

from glycophorin A (abstract). Melnyk teach the Tar-1 helix as the oligomeric determinant for the Tar protein and that the approach can be used to elucidate details of transmembrane domain folding (abstract). Melnyk teach that the E. coli aspartate receptor transmembrane domain peptides were designed based on predictions of which residues occur in the protein transmembrane segment (see Table 2 caption). Melnyk teach that the peptides were synthesized with N and C-terminal lysines (page 11109 2nd column and Table 2). Melnyk teach the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK (Tar (TM-1) 6K-Tar-1). Melnyk teach that the peptide was used in a composition (Figures 3-4 for example).

Melnyk does not expressly teach at least 2 D-amino acids in the peptide.

Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Thus Melnyk recognizes a problem in the art. Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments from glycophorin A (abstract).

Bolognesi teach peptides which correspond to an HIV transmembrane protein (abstract, claim 1 for example, column 1 lines 37-39). Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration into the peptides (claim 12).

Gerber report studies using the glycophorin A (GPA) transmembrane domain (abstract, Table 1). Gerber teach the incorporation of D-amino acids in the peptide and state that an advantage of D-amino acids is that they prevent protease degradation and result in a longer life-span of the peptide (page 494 last paragraph). Gerber teach that for the GPA analogues that all

D GPA analogues exhibit the same binding affinities, insertion, and localization as the all L (page 492 last paragraph of 1st column). Gerber teach that GPA helix-helix recognition within the membrane is chirality-independent (abstract).

Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Thus Melnyk recognizes a problem in the art. Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments from glycophorin A (abstract). Both Bolognesi and Gerber teach what is well-known in the art – the incorporation of D-amino acids for increased stability. Further, both Bolognesi and Gerber provide the teaching for transmembrane protein fragments and in fact Belnyk even discusses the specific protein (GPA) as taught by Gerber. Since Gerber teach that an advantage of D-amino acids is that they prevent protease degradation and result in a longer life-span of the peptide one would be motivated to incorporate D-amino acid isomers into the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK). Since Bolognesi expressly teach the incorporation of one or more D-amino acids one would be motivated to include any number of D-amino acids such as 2. Since Gerber teach that for the GPA analogues that all D GPA analogues exhibit the same binding affinities, insertion, and localization as the all L (page 492 last paragraph of 1st column) and teach that GPA helix-helix recognition within the membrane is chirality-independent (abstract) one would have a reasonable expectation of success.

Thus the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) with multiple (for example 2) D-isomers reads on claims 1 of the instant invention. It is noted that

claims 1-2 use 'comprising' language with respect to the length of the peptide. Since the peptide of Melnyk is 30 amino acids in length the limitations of claim 2 for example are met. Since Melnyk teach the peptide from E. coli aspartate receptor (abstract) the limitations of claims 3,18 are met. Since the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) comprises SEQ ID NO:20 the limitations of claim 19 are met. Since the peptide of Melnyk includes KKK at both the N and C terminus the limitations of claim 20 are met. Since the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) comprises SEQ ID NO:22 the limitations of claim 21 are met as currently interpreted. Since Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12) and there are a finite number of amino acids in the peptide of Melnyk it would have been obvious to optimize the location and number of D-amino acids in the peptide. Since Melnyk teach the peptide was used in a composition (Figures 3-4 for example) the limitations of claim 22 are met.

Taken together, the references teach common subject matter – peptides of transmembrane domains. Further, Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). The claims would have been obvious because the technique of improving a particular class of peptides (via the inclusion of D-isomers) was part of the ordinary capabilities of a person of ordinary skill in the art in view of the teaching of the technique for improvement in other situations. In the instant case, both Bolognesi and Gerber teach what is well known in the art - the inclusion of D-isomers into peptides of transmembrane domains.

Although unclear (see 112 2nd), for purposes of examination the phrase 'diastereomeric active fragments, derivatives, analogs or salts thereof' has been given the broadest reasonable

interpretation. In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids.

Although unclear (see 112 2nd), for purposes of examination claim 19 has been interpreted such that SEQ ID NO:20 can include D-amino acids.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sal-Man et al (JMB v344 2004 pages 855-864 as cited in IDS 9/8/08) and ScienceDirect web page (retrieved from http://www.sciencedirect.com/science?_ob=PublicationURL&_cdi=6899&_pubType=J&_acct=C000055109&_version=1&_urlVersion=0&_userid=2502287&md5=d82644f529ee8e69fccbfcb9d61c2f4c&jchunk=350#350 on 4/3/09 4 pages) and Bolognesi et al (US 5,464,933 as cited in IDS 9/8/08).

As discussed above (see priority section) claims 18-21 are searched based on a priority date of 12/22/04.

It is noted that Sal-Man et al is cited in the IDS 9/8/08. However, only the year is listed in the citation. ScienceDirect web page is cited to show (see page 2 left hand column) that Sal-Man et al (i.e. v344 pages 855-864) was publicly available Nov 26 2004 and thus is prior art.

Sal-Man teach peptides of the transmembrane domain of the E. coli aspartate receptor that include all L and all D versions (abstract). Specifically Sal-Man teach the peptide KKKMVLGVFALLQLISGSLKKK (Tar-1 WT Table 1) in which the peptide is either all L or all D amino acids. Sal-Man teach that the all D version has activity similar to the all L version (page 858 discussion).

Sal-Man does not expressly teach a 'diastereomeric peptide' as defined in the instant invention (page 12) to comprise L-amino and D-amino residues.

Bolognesi teach peptides which correspond to an HIV transmembrane protein (abstract, claim 1 for example, column 1 lines 37-39). Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12). Thus Bolognesi teach what is well known in the art.

Since Bolognesi expressly teach the incorporation of one or more D-amino acids one would be motivated to include any number of D-amino acids such as 2. Taken together one would be motivated to make the peptide of Sal-Man (KKKMVLGVFALLQLISGSLKKK) in which there are 2 D-amino acids. Since Sal-Man teach the peptide from E. coli aspartate receptor the limitations of claim 18 are met. Since the peptide of Sal-Man (i.e.

KKKMVLGVFALLQLISGSLKKK) comprises SEQ ID NO:20 the limitations of claim 19 are met. Since the peptide of Sal-Man includes K residues at both the N and C terminus the limitations of claim 20 are met. Since the peptide of Sal-Man comprises SEQ ID NO:23 the limitations of claim 21 are met as currently interpreted. Since Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12) and there are a finite number of amino acids in the peptide of Sal-Man it would have been obvious to optimize the location and number of D-amino acids in the peptide.

The claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Although unclear (see 112 2nd), for purposes of examination the phrase 'diastereomeric active fragments, derivatives, analogs or salts thereof' has been given the broadest reasonable interpretation. In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids.

Although unclear (see 112 2nd), for purposes of examination claim 19 has been interpreted such that SEQ ID NO:20 can include D-amino acids.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654